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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/620,561	07/20/2000	Michael C. Keifer	22441.00001	2898

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EXAMINER
LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 11/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/620,561	Applicant(s) KEIFER ET AL.	
	Examiner Robert Landsman	Art Unit 1647	

-- The MAILING DATE of this communication app ars on the cover sh et with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-25,31-35,37 and 40-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22,23,25,31-35,37 and 40-47* is/are rejected.

7)☒ Claim(s) *24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparisons A-H* .

DETAILED ACTION

1. Formal Matters

A. Sequence Amendment B, filed 9/9/02, has been entered into the record.

B. Claims 22-47 are pending in this application and were subject to restriction in Paper No. 4 dated 7/1/02. In Paper No. 5, Applicants elected Group I, claims 22-25, 31-35, 37 and 40-47. Since Applicants did not provide a traversal with their election, this response will be treated as an election without traverse. This restriction is deemed proper and is, therefore, made FINAL.

2. Specification

A. In Amendment A, filed 7/20/00, Applicants amended the first line of the specification to recite that the present application is a divisional of 08/479,992. However, it appears that the correct application number is 08/439,992. This typographical error has been corrected by the Examiner.

B. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The claims are drawn toward compositions comprising polynucleotides encoding hFGF and methods of using these polynucleotides.

3. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 22, 23, 25, 31-35, 37, 40-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions consisting of, and methods of using a polynucleotide encoding SEQ ID NO:1, does not reasonably provide enablement for compositions consisting of, and methods of using polynucleotides encoding hFGFr other than SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence

of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to claiming compositions consisting of, and methods of using all polynucleotides encoding hFGFr other than those encoding SEQ ID NO:1 which are identifiable using the claimed primers (SEQ ID NO:7 and 8). Nucleic acid molecules obtained using primers of SEQ ID NO:7 and 8 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to those encoding SEQ ID NO:1 and would encode for proteins with one or more amino acid substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:1.

The only limitation of the polynucleotides of the present invention is that they must be identified using primers of SEQ ID NO:7 and 8. Applicants provide no guidance or working examples of nucleic acid molecules which are obtained using primers of SEQ ID NO:7 and 8 other than those encoding SEQ ID NO:1, nor do they provide a *function* of these nucleic acid molecules, or of the proteins which they encode. Applicants have provided no guidance as to what critical residues are required to maintain the functional characteristics of a hFGFr other than that of SEQ ID NO:1. Furthermore, it is not predictable to one of ordinary skill in the art how to make a functional hFGFr other than that of SEQ ID NO:1.

In summary, the breadth of the claims is excessive with regard to Applicants claiming all compositions consisting of, and methods of using all polynucleotides encoding hFGFr other than those encoding SEQ ID NO:1. There is also a lack of guidance and working examples of these nucleic acid molecules and encoded proteins as well as any teachings as to which residues are critical for hFGFr function. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to identify or make a functional hFGFr other that that of SEQ ID NO:1 leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

4. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 22, 23, 25, 31-35, 37, 40-47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Nucleic acid molecules encoding hFGFr which are identifiable by using primers of SEQ ID NO:7 and 8 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to said polynucleotides (e.g those encoding SEQ ID NO:1) and would encode proteins

with one or more amino acid substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:1.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although these types of changes are routinely done in the art, the specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

The specification provides a written description of only SEQ ID NO:1. No other species are described, or structurally contemplated, within the instant specification. Therefore, one skilled in the art cannot reasonably visualize or predict critical nucleic acid residues which would structurally characterize the genus of nucleic acids encoding the genus of hFGFr proteins claimed, because it is unknown and not described what structurally constitutes any different nucleic acids encoding hFGFr, or nucleic acids encoding hFGFr from any different species, which are further not described; thereby not meeting the written description requirement under 35 USC 112, first paragraph.Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:1 alone is insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

5. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22, 23, 25, 31-35, 37, 40-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 22, 23, 25, 31-35, 37, 40-47 are vague and indefinite since the metes and bounds of "immunoglobulinlike domains" are not known, nor is any definition provided in the specification. Applicants are stating that a requirement of the claimed composition is that the FGFr must comprise three immunoglobulin-like domains. However, Applicants have not defined what domains are considered to be "like" an immunoglobulin domain, or which immunoglobulin domains the hFGFr of the present invention must be "like." In addition, though not the basis for a rejection, Applicants may wish to hyphenate the term "immunoglobulinlike" (i.e. "immunoglobulin-like"), though the prior art recites this term with and without a hyphen.

B. Claims 22, 23, 25, 31-35, 37, 40-47 are vague and indefinite since the claim recites "conditions that permit hybridization." It is not known what these conditions are. Nucleic acid molecules which hybridize under conditions of "low" stringency would not necessarily hybridize under conditions of "high" stringency. Furthermore, not all conditions of "high" or "low" stringency, for example, are the same. Therefore, it is required that Applicants amend the claims to recite the exact hybridization conditions without using indefinite phrases such as "*for example*" **without adding new matter**.

C. Claim 46 is confusing since it recites "extracellular human fibroblast growth factor." It is not known what the difference is between an "extracellular" FGF and the wild-type FGF.

6. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 22, 23, 25, 31-35, 37 and 40-47 are rejected under 35 U.S.C. 102(a) as being anticipated by Johnson et al. (Mol. Cell Biol. 10:4728-4736, 1990). The claims recite a composition comprising a hFGFr having three immunoglobulin-like domains wherein the encoding polynucleotide is obtainable by using primers of SEQ ID NO:7 and 8. The claims also recite methods of isolating said polynucleotide as well as host cells and methods of making the hFGFr protein. Johnson et al. teach a protein which is 99.6% identical to SEQ ID NO:1 (Sequence Comparison B) and wherein the encoding polynucleotide has 100%

identity to SEQ ID NO:7 and 8 (Sequence Comparisons C and H). Due to the 100% overlap between the protein of Johnson et al. and SEQ ID NO:7 and 8, it would be expected that the DNA encoded for by the protein of Johnson et al. would hybridize to SEQ ID NO:7 and 8 even under the most highly stringent conditions. The construction of plasmids comprising the polynucleotides encoding numerous hFGFr clones, including a three-immunpglobulinlike-domain, as well as methods of isolating these polynucleotides, and the production of host cells is also taught by Johnson et al. ("Materials and Methods" and "Results"). In absence of evidence to the contrary, it would be expected that the plasmids used to express the hFGFR protein would have an origin of replication. Finally, Johnson et al. teach a method of producing hFGFr (under "Injection of oocytes" on page 4729). The fact that oocytes were transferred and the supernatants were removed meets the claimed limitations of "recovering the polypeptide from the medium." Regardless of whether or not Johnson et al. actually recovered and purified the isolated protein from the medium and cells, Johnson et al. still meet the limitation of the claims of producing a hFGFr.

B. Claims 22, 23, 25, 31-35 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Ruta et al. (Oncogene 3:9-15, 1988). The claims recite a composition comprising a hFGFr having three immunoglobulin-like domains wherein the encoding polynucleotide is obtainable by using primers of SEQ ID NO:7 and 8. The claims also recite methods of isolating said polynucleotide as well as host cells and methods of making the hFGFr protein. Ruta et al. teach a protein which is 99.6% identical to SEQ ID NO:1 (Sequence Comparison B) and wherein the encoding polynucleotide has 100% identity to SEQ ID NO:7 and 8 (Sequence Comparisons D and E). Due to the 100% overlap between the protein of Ruta et al. and SEQ ID NO:7 and 8, it would be expected that the DNA encoded for by the protein of Ruta et al. would hybridize to SEQ ID NO:7 and 8 even under the most highly stringent conditions.

C. Claims 22, 23, 25, 31-35, 37 and 40-47 are rejected under 35 U.S.C. 102(a) as being anticipated by Dionne et al. (EMBO J. 9(9):2685-2692, 1990). The claims recite a composition comprising a hFGFr having three immunoglobulin-like domains wherein the encoding polynucleotide is obtainable by using primers of SEQ ID NO:7 and 8. The claims also recite methods of isolating said polynucleotide as well as host cells and methods of making the hFGFr protein. Dionne et al. teach a protein which is 99.6% identical to SEQ ID NO:1 (Sequence Comparison B) and wherein the encoding polynucleotide has 100% identity to SEQ ID NO:8 (Sequence Comparison F). Due to the 100% overlap between the protein of Dionne et al. and SEQ ID NO:8, combined with the fact that this protein is 99.6% identical to that of SEQ

ID NO:1 of the present invention as well as to that of Johnson et al. and Ruta et al. (see above rejections under 35 USC 102), it would be expected that the DNA encoded for by the protein of Dionne et al. would hybridize to SEQ ID NO:8 as well as SEQ ID NO:7 even under the most highly stringent conditions or would at least encode a hFGFr having a sequence substantially the same as that which hybridizes to SEQ ID NO:7 and 8. The construction of plasmids comprising the polynucleotides encoding hFGFr (i.e. flg), as well as methods of isolating these polynucleotides, the production of host cells and a method of producing hFGFr is also taught by Dionne et al. ("Cloning of human flg and bek" on page 2686 and "Expression of bek and flg in transfected cells" on page 2687). In absence of evidence to the contrary, it would be expected that the plasmids used to express the hFGFR protein would have an origin of replication.

D. Claims 22, 23, 25, 31-35 and 37 are rejected under 35 U.S.C. 102(a) as being anticipated by Isacchi et al. (Nucleic Acids Res. 18(7):1906, 1990). Isacchi et al. teach a polynucleotide encoding a polypeptide which is 99.6% identical to SEQ ID NO:1 of the present invention (Sequence Comparison A). Due to the high degree of overlap between the protein encoded for by the polynucleotide of Isacchi et al. and that of the present invention, it would be expected that the polynucleotide of Isacchi et al. would hybridize to SEQ ID NO:7 and 8, or would at least encode a hFGFr having a sequence substantially the same as that which hybridizes to SEQ ID NO:7 and 8.

7. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claims 40-47 rejected under 35 U.S.C. 103(a) as being unpatentable over Isacchi et al. in view of Dionne et al. The claims recite host cells and methods of making the hFGFr protein. The teachings of Isacchi et al. and Dionne et al. are recited in the above rejection under 35 USC 102. Isacchi et al. do not teach the host cells or a method of producing an hFGFr polypeptide. However, the production of host cells and a method of producing hFGFr is taught by Dionne et al. ("Cloning of human flg and bek" on page 2686 and "Expression of bek and flg in transfected cells" on page 2687).

Therefore, it would have been obvious to one of ordinary skill at the time of the present invention to have substituted the cDNA of Isacchi et al. for the cDNA of Dionne et al. and to have transfected the host cells of Dionne et al. to produce the hFGFr protein since both Isacchi et al. and Dionne et al. teach hFGFr. One of ordinary skill in the art would have been motivated to make this substitution in order to express the protein encoded by the introduced DNA in a host cell to perform ligand binding and functional assays, or to further characterize the protein. There would have been a reasonable expectation of success for a person of ordinary skill in the art to make this invention since these techniques are widely used in the art and are highly successful. The present invention, therefore, is *prima facia* obvious over the above references in the absence of evidence to the contrary.

B. Claims 40-47 rejected under 35 U.S.C. 103(a) as being unpatentable over Ruta et al. in view of Dionne et al. The claims recite host cells and methods of making the hFGFr protein. The teachings of Ruta et al. and Dionne et al. are recited in the above rejection under 35 USC 102. Ruta et al. do not teach the host cells or a method of producing an hFGFr polypeptide. However, the production of host cells and a method of producing hFGFr is taught by Dionne et al. ("Cloning of human flg and bek" on page 2686 and "Expression of bek and flg in transfected cells" on page 2687).

Therefore, it would have been obvious to one of ordinary skill at the time of the present invention to have substituted the cDNA of Ruta et al. for the cDNA of Dionne et al. and to have transfected the host cells of Dionne et al. to produce the hFGFr protein since both Ruta et al. and Dionne et al. teach hFGFr. One of ordinary skill in the art would have been motivated to make this substitution in order to express the protein encoded by the introduced DNA in a host cell to perform ligand binding and functional assays, or to further characterize the protein. There would have been a reasonable expectation of success for a person of ordinary skill in the art to make this invention since these techniques are widely used in the art and are highly successful. The present invention, therefore, is *prima facia* obvious over the above references in the absence of evidence to the contrary.

8. Other Art of Interest

A. According to Sequence Comparison B which accompanies this Office Action, it appears that Itoh et al. (BBRC 169(2):680-685, 1990) teach a protein which is 99.6% identical to SEQ ID NO:1 of the present invention. However, Itoh et al. state that this protein comprises only two immunoglobulinlike domains and not three, as claimed by the present invention. therefore, no rejection under 35 USC 102 is being made.

9. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
November 01, 2002